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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/963,656	11/03/1997	CRAIG J. GERARD	LKS9405A2Z	1351

7590

01/28/2002

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 01/28/2002

25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/963,656

Applicant(s)

GERARD ET AL.

Examiner

Joseph F Murphy

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38,39,49-51,53,55 and 57-150 is/are pending in the application.
- 4a) Of the above claim(s) 59-67 and 104-118 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38,39,49-51,53,55,57,58,68-103 and 119-150 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>21</u> | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1646

DETAILED ACTION

Continued Prosecution Application

The request filed on 11/15/2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08963656 is acceptable and a CPA has been established. An action on the CPA follows.

Formal Matters

Claims 38-39, 49-51, 53, 55, 59-62, 65, 67, 69-73, 75, 77-81 were amended, and new claims 87-150 were added, in Paper No. 22, 9/17/2001. Claims 38-39, 49-51, 53, 55, 57-150 are pending. Claims 59-67 and new claims 104-118 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 38-39, 49-51, 53, 55, 57-58, 68-103, 119-150 are pending and under consideration.

Response to Amendment

Applicant's amendments and arguments filed 9/26/2000 have been fully considered but they are not persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-39, 49-51, 53, 55, 57-58, 75-76, 81, 86, 89, 90, 91, 92-103, 143-145, 148-150 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

Art Unit: 1646

invention, for reasons of record set forth in paper No. 14, 8/4/99. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant argues that the amendments more clearly define the invention by recitation of structural and functional features on mammalian C-C chemokine receptor 3 protein.

However, the specification discloses antibodies and antigen-binding fragments which bind to a human C-C chemokines receptor 3 protein. The antibody which binds to this amino acid sequences meets the written description and enablement provisions of 35 U.S.C. 112, first paragraph. However, the indicated claims are directed to encompass antibodies and antigen-binding fragments which bind mammalian homologues of the disclosed amino acid sequences having undisclosed amino acid sequences which correspond to sequences from other species. None of the claimed antibodies or antigen binding fragments which bind mammalian homologues of the disclosed amino acid sequences having undisclosed amino acid sequences which correspond to sequences from other species meet the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. V. Makurhar, 19 USPQ2d 1111, makes clear that applicant must convey with reasonable clarity to those skilled in the art, as the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry whatever is now claimed (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (See Vas-Cath Inc. V. Makurhar, page 1116.).

Art Unit: 1646

With the exception of antibodies and antigen-binding fragments which bind to a human C-C chemokine receptor 3 protein the skilled artisan can not envision the detailed chemical structure of the mammalian homologues of the disclosed amino acid sequences having undisclosed amino acid sequences which correspond to sequences from other species, and therefore the encompassed antibodies or antigen binding fragments also cannot be envisioned and thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that is part of the invention and reference to a potential method for isolating it, The antibody and antigen binding fragment itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.* 18 USPQ 2d 1016. One can not describe what one has not conceived. See *Fiddes v. Baird* 30 USPQ 2d 1481, 1483. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

Art Unit: 1646

Claims 38-39, 49-51, 53, 55, 57-58, 68-103, 119-150 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in paper No. 14, 8/4/99. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The amended claims encompass antibodies and antigen-binding fragments which bind to a C-C chemokines receptor 3 protein that are encoded by a nucleic acid that hybridizes under moderate or high stringency conditions to a second nucleic acid consisting of the nucleotide sequence of SEQ ID NO:1, 3 or 5. According to the specification (page 30, lines 13-19) the term variant means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to SEQ ID NO: 1, 3, or 5. The specification and claim do not indicate what distinguishing attributes are shared by the members of the genus. The specification and claim encompass a large number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 1, 3 or 5. Thus, the scope of the claims include antibodies and antigen binding fragments directed to numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim provide insufficient guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. Insufficient common structural

Art Unit: 1646

attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to sufficiently describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, antibodies and antigen binding fragments which bind SEQ ID NO: 1, 3, and 5 are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-39, 49-51, 53, 55, 57-58, 68-103, 119-150 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 38, 49, 53, 70-71, 73, 75, 92-93, 99-100, 119-120, 125, 135-136, 144-149 recites the terms either "moderate" or "high" stringency conditions, which are conditional terms and render the claims indefinite. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be either "moderate" or "high" stringency conditions. Claims 39, 50-51, 55, 57-58, 69, 72, 74, 76-88, 90-91, 94-98, 101-103, 121-124, 127-134, 137-143, 150 are rejected insofar as they depend on the recitation in claims 38, 49, 53, 70-71, 73, 75, 92-93, 99-100, 119-120, 125, 135-136, 144-149 of either "moderate" or "high" stringency conditions.

Claim Rejections - 35 USC § 103

Claims 38-39, 49-50, 70-71, 73, 75 rejected under 35 U.S.C. 103(a) as being unpatentable over Yamagami et al (1994) in view of Lerner (1982) and Harlow et al. (1988).

The rejection was set forth in Paper No. 9, 12/16/1998 and Paper No. 14, 8/4/1999. Essentially, the rejection is on the basis that Yamagami et al. discloses the cDNA cloning, the predicted amino acid sequence and functional expression of a human monocyte chemoattractant protein 1 receptor (page 1156, see abstract; page 1159, Figure 1; page 1161, Figure 3), the reference receptor having a stretch of 10 amino acids identical (residues 140-148) with the amino acid sequence depicted in SEQ ID NO:2 of the instant application, these 10 residues not being part of the transmembrane domain Lerner teaches the production of antibodies from known polypeptides, wherein the antibody can have predetermined specificity and in addition can be of a single specificity (i.e. a monoclonal) (see abstract, page 592; and first paragraph). Lerner also teaches that antibodies made against a predetermined peptide are useful in studying the protein conformation of the intact protein from which the immunizing peptide was cleaved from (column 2, page 594, last 8 lines on page). Further Harlow et al. teach that peptides of six residues in length will consistently elicit antibodies that bind to the original protein (page 76, third paragraph, especially lines 21-22). Therefore, it would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to use the amino acid sequences taught by Yamagami et al., to produce monoclonal and polyclonal antibodies with a predetermined specificity as taught by Lerner, which would be useful in understanding the conformational changes the receptor undergoes during activation by a natural ligand.

Applicant argues: i) that there are not 6 amino acids in common between the extracellular regions of the C-C chemokine receptor 3 protein and the prior art receptor, and that inspection of the alignment in view of the teachings of Yamagami et al. reveals that the regions of amino acid identity are clustered in the transmembrane and intracellular portion of the two receptors.

However, the claims are not directed to antibodies to the extracellular region of C-C chemokine receptor 3 protein, and only limit the antibody to having a binding specificity for C-C chemokine receptor 3 protein. Additionally, the binding of an antibody to the intracellular region of the receptor would inhibit a function associated with binding of ligand to the receptor, i.e. transduction of signal from the receptor to the G protein heterotrimer.

Applicants additionally argue that ii) the claimed invention would be considered nonobvious because the combined teachings of the cited references do not teach the desirability or direct the skilled person to prepare antibodies using peptides derived from regions of C-C chemokine receptor 3 protein which have sequence identity to other chemokine receptors

However, the Lerner reference teaches the making of antibodies to several different domains in a polypeptide to study the various domains fate (page 594, column 2, second paragraph) and function (page 595, column 1, first full paragraph). Additionally, Lerner et al. teaches the use of chemically synthesized peptides (Ibid.) to generate antibodies, thus antibodies can be to any domain, not only the extracellular domains.

Applicant further argues that iii) the claimed invention would be considered nonobvious because the combined teachings of the cited references do not teach the desirability or direct the skilled person to prepare antibodies using peptides derived from regions of C-C chemokine

Art Unit: 1646

receptor 3 protein which have sequence identity to other chemokine receptors, and that the primary use of antibodies is to distinguish a selected polypeptide from other proteins based upon antibody binding and to allow for specific targeting of the polypeptide for therapeutic, diagnostic or research applications.

However, the claims do not include a limitation whereby the antibody is directed to peptides derived from regions of C-C chemokine receptor 3 protein which have sequence identity to other chemokine receptors. Additionally, while Applicant has argued that the primary use of antibodies is for selection of a specific polypeptide, the claims only recite that the antibody have a "binding specificity" to C-C chemokine receptor 3 protein, not that it bind exclusively to C-C chemokine receptor 3 protein. Furthermore, an additional function, as discussed in Lerner, is to track function of peptide domains of a polypeptide, not only for isolation of specific polypeptides.

Conclusion

No claim is allowed.

Art Unit: 1646

Advisory Information

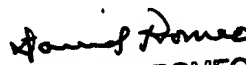
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 17, 2002


DAVID S. ROMEO
PRIMARY EXAMINER